Differences in spatio-temporal distribution of the visual P3b event-related potential between young men and women

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Here, we evaluated the P3b potential evoked in a visual two-stimulus oddball paradigm. The experiment was conducted in 20 healthy students (23.1±1.1 years, 10 women), using a 32 channel electroencephalography (EEG) montage system. The paradigm included geometric figures; a black square on a white background as a target and a white circle on a black background as a standard stimulus. We examined the maximal amplitude and latency of the P3b component at 18 electrode sites, as well as, temporal changes of scalp voltage distribution. We observed a non-equal spatial distribution of the visual ERP (event related potentials) waveforms on the scalp surface, with the highest P3b waveform observed over midline parietal areas and the lowest over frontal regions. Moreover, the spatial distribution of ERP signal on the scalp surface was more lateralized towards the right side in men and more centralized in women. Gender-related differences in P3b amplitude and latency were observed only in left hemisphere. Differences in P3b between men and women observed in our study arose not only from different P3b amplitudes and latencies, but also from the speed and character of P3b waveform fall, resulting in spatio-temporal amplitude changes. Moreover, the spatial distribution of the P200 potential also changed on the scalp differently in men and women. These results suggest that gender-related differences evoked in visual two-stimulus oddball paradigm, which engage attention processes, are complex and include spatio-temporal changes in P3b waveform generation, distribution, and suppression across the scalp.

Key words: visual P3b, event related potentials, spatio-temporal ERP distribution, gender

INTRODUCTION

The P300 is one of the most extensively studied event-related brain potentials (ERPs) and is thought to account for information processing mechanisms of attention allocation and immediate memory, including context updating, working memory storage, and task-related memory operations (Ibanez et al., 2012; Dehaene et al., 2014; Chapman et al., 2015; Rutikku et al., 2015). According to Polich and Criado (2006), in a single-stimulus oddball task, a target stimulus is presented infrequently in time with no other stimuli (Polich and Criado, 2006). In a standard two-stimulus oddball paradigm, in contrast, an infrequent target occurs in the background of frequent standard stimuli. In a three-stimulus oddball task, a target is presented infrequently in a background of frequently occurring standard stimuli and infrequently occurring distracter stimuli. The P3a potential has a maximal amplitude over central/parietal region, and is elicited by an infrequent stimulus in the absence of a task. The name, P3a, distinguishes it from the other subcomponent of P300 waveform – the task-relevant target P3b potential. In contrast, a “novel P300” potential is elicited by non-repeated, perceptually novel distracter stimuli, presented with target and standard stimuli and is thought to index initial signal evaluation. The P300 maximum am-
The P3b waveform is generated as a result of memory comparison wherein a current stimulus is evaluated in the context of the previous stimuli—a process called the “context updating approach” (Delplanque et al., 2005; Polich and Criado, 2006; Polich, 2007). These memory storage operations are initiated in the hippocampal formation and updated outputs are subsequently transmitted to the parietal cortex (Knight, 1996; Squire and Kandel, 1999). Amplitude of the P3b component is sensitive to the amount of attentional resources engaged during task performance, and variation in P3b amplitude is assumed to reflect the degree or quality with which information is processed (Polich and Herbst, 2000; Lukács et al., 2016). Latency of the P3b component is thought to reflect stimulus classification speed, which is proportional to the time required to detect and evaluate a target stimulus. Thus, P3b latency may be a sensitive temporal measure of the neural activity underlying the processes of attention allocation and immediate memory (Polich and Herbst, 2000).

The P3b component has many potential generators, which form a widespread neuronal network (Comerchero and Polich, 1998; 1999; Polich and Criado, 2006; Zheng et al., 2015). P300 generation (including P3b) has been shown to include regions of the superior and inferior frontal lobe, middle temporal gyrus, parietal lobe, temporoparietal junction, lateral prefrontal areas, and the cingulate gyrus (Bocquillon et al., 2011; Sabeti et al., 2016). Moreover, regions of the inferior parietal lobe, prefrontal, and cingulate cortices were found to be involved in the generation of target-elicited P3b (Bocquillon et al., 2011; Volpe 2007).

Gender is one factor that may influence ERP waveforms related to attention processes. However, despite the wide range of studies, there is still no consensus regarding gender-related differences in the P3b waveform. In a normative study of P3a and P3b from a large sample using a visual three-stimulus ERP oddball paradigm, Conroy and Polich (2007) obtained larger and later P3a and P3b components from females than from male subjects. In addition, P3b amplitude was negatively correlated with P3b latency over right frontal areas, and was positively correlated with response time (RT) over right parietal areas (Conroy and Polich, 2007). Hoffman and Polich (1999) also obtained larger P300 components in women than in men in a standard oddball task, as well as in a single-stimulus paradigm with visual and auditory stimuli. These results suggest that the observed gender differences arose from differences in corpus callosum size and inter-hemispheric transmission efficacy (Hoffman and Polich, 1999). Jaušovec and Jaušovec (2009a) studied gender-related differences in visual and auditory processing of verbal and figural task. They found shorter RTs in a visual task as well as higher amplitudes for both P1 and P3b in women than in men (Jaušovec and Jaušovec, 2009a). The authors concluded that these results reflected an enhancement in matching process in women, potentially subserved by more distinct sensory information and greater allocation resources that improve perceptual accuracy (Jaušovec and Jaušovec, 2009a). However, despite the fact that the measurements were performed at 22 frontal, central, and parietal EEG electrode localizations, the paper presents ERP results averaged across all electrodes. The authors also found higher P3b amplitudes in women than in men in a simple visual and auditory oddball paradigm task (Jaušovec and Jaušovec, 2009b). Finally, both main effects of gender and gender-by-location interactions were reported; however post hoc results were not reported that would reveal the electrode site(s) that show significant gender effects. No gender-related differences were observed for ERP latencies. In studies conducted by Steffensen et al. (2008), RTs to target stimuli did not differ between genders (Steffensen et al., 2008). Further, amplitude of P3b was greater in women than in men and the latency didn’t differ; however, the analysis was limited to five electrode sites (Oz, O1, O2, P3 and P4). Alternatively, Vaquero et al. (2004) obtained higher amplitudes for both P1 and P3b in men compared to women, whereas women showed higher amplitudes in the temporal N1 than did men. In that same study, the amplitude of the P3 potential over frontal/central regions was higher in men than in women, and men presented a gender-specific right frontal functional asymmetry that was not present in women in a visual-spatial attention task (as measured at F3, F4, C3, C4, P3, P4, T5, T6, O1, O2 electrodes). The authors concluded that those components were related with the modulation of visual processing via effects of spatial attention (Vaquero et al., 2004). On the other hand, Sangal and Sangal (1996) did not find differences in P300 amplitudes or latencies by gender, modality, or side of scalp. In addition, there were no significant topographical differences in P300 amplitudes or latencies were noted by gender, age-group, modality, or side of scalp in auditory and visual P300 recordings.
(Sangal and Sangal, 1996). Shelton et al. (2002) found no significant main effect of gender, nor any significant gender-interactive effects in ERP responses (i.e., P3 amplitude and latency) in visual and auditory two-stimulus simple tasks, as measured at electrode Cz. In a facial affect recognition on the bimodal auditory-visual P300 task, Morita et al. (2001) found no gender differences in P3 amplitudes nor latencies for neutral faces, measured at midline electrodes (Fz, Cz, Pz, Oz), C3 and C4 (Morita et al., 2001). Tsolaki et al. (2015) observed no gender-related differences in P3b amplitude and latency in simple two-tone oddball study, measured at electrode Pz (Tsolaki et al., 2015). However, Tsolaki et al. (2015) obtained faster responses while retaining the same error level in men than in women. Next, based on a sLORETA source localization analysis, they found that females had maximum intensity of the P3b component in the frontal lobe, whereas intensity was maximal in the temporal lobe among males. Together, differences in obtained results could be due to methodological discrepancies, for e.g., different tasks, type of responses required, time windows used. Many of the reviewed studies were conducted using only a few electrode sites, for e.g., along midline areas or only from a small area such as parietal regions. Moreover, prior investigations were focused primarily on comparing the amplitude and latency values and/or source localization analysis. Therefore, there is need for an extended analysis of a target elicited P3b potential in a group of young males and females.

To our best knowledge, the present study is the first to investigate spatio-temporal gender-related differences in visual P3b evoked using a standard oddball experiment, in such a broad perspective. We not only analyzed P3b maximal amplitude and latency across 18 channels, but also considered gender differences at each electrode site, hemispheric and midline differences, and correlations between these parameters and with behavioral data. We also evaluated differences in scalp voltage distribution after onset of the target stimuli and performed a statistical analysis of ERP time courses using nonparametric permutation cluster analysis. The latter is an additional novel aspect of this study, and may provide deeper insights into the current knowledge of gender-based differences during the generation, propagation, and decline of the P3b waveform.

METHODS

Participants

The present experiment included 20 students (23.1±1.1 years, 10 women). All students were right-hand-
1000 ms inter-stimulus interval, 20% target and 80% standard stimulus probabilities. The total number of stimulus presentations was 300, including 240 standard and 60 target stimuli. Advanced Source Analysis system ASA-Lab (ANT Neuro) with ASA v.4.8 software was used for data acquisition and analysis.

**Apparatus and recording**

Data processing

Recorded EEG signals were filtered using a Butterworth type band-pass filter, based on the FFT method, with frequencies 0.01–30 Hz and filter slope 24 dB/oct. Signals with amplitude over ±75μV were detected and removed from the analysis. Electrooculography artifacts from eye movement were corrected using a PCA algorithm. After baseline correction and detrending using a 100 ms prestimulus time window, analyzed EEG epochs were averaged within a 1000 ms time window. In the final step of the analysis, individual ERP waveforms were grand averaged to obtain mean ERPs from the whole experimental group. Mean (± standard deviation) number of standard and target stimuli after data processing were: 160±32 and 40±8 in women and 164±51 and 40±13 in men, respectively. The acquisition as well as the processing of EEG signals were performed according to International Federation of Clinical Neurophysiology (IFCN) Guidelines for eliciting, recording, and quantifying mismatch negativity, P300, and N400 (Duncan et al., 2009). To extract the signal changes, which are related to attention processes, differences in ERP waveforms (i.e., target-standard) were calculated. All further analyses were performed on these difference waveforms.

**Statistical analysis**

Statistical analysis was performed on both behavioral and electrophysiological data. For each analyzed group, the assumptions for the use of parametric tests were checked with the use of appropriate tests. In particular, Shapiro-Wilk’s test was used to check the normality of the data distributions, and Levene’s test was used to check variation homogeneity. When the data did not fulfill assumptions required for parametric tests, nonparametric equivalent tests were used. Behavioral data (RT and percentage of correct hits) as well as electrophysiological data (P3b amplitudes and latencies) were compared between men and women by means of two-tailed independent samples t-test. Hemispheric differences were calculated using two-tailed paired samples t-tests. The differences between channels were assessed by means of repeated-measures ANOVA with channel as the within-subject factor and gender as a between-subjects factor. Significant ANOVA results were followed by post hoc comparisons performed with Bonferroni correction. Sphericity of the data was checked by means of Mauchley’s test. Greenhouse-Geisser, Huynh-Feld, and lower-bound corrections for violation of sphericity were used, as appropriate, followed by multivariate Wilks, Pillai, Hotelling-Lawley, and Roy tests for repeated-measures ANOVA (as an additional confirmation of obtained corrected univariate results). For correlation analysis, Pearson Bivariate correlation was used for normally distributed data, and Spearman’s rank-order correlation for data which didn’t meet this criterion. In all analyses, P<0.05 was regarded as statistically significant. The ERPs from men and women were also analyzed by means of non-parametric permutation cluster test with 2000 permutations for solving the MCP (multiple comparison problem) using MNE (Python) software, according to Maris and Oostenveld (2007).

**RESULTS**

**Behavioral data**

Average RTs, characterized by the time delay between the rare stimulus onset and the button press, for men and women were 350±25 ms and 364±43 ms, respectively. RTs did not differ between genders (t_{18}=-0.9, P=0.38). Similarly, correct hits did not differ between men (97.8±2.6%) and women (99.0±1.4%, t_{18}=-1.2, P=0.24).

**Electrophysiological data**

The grand averaged difference in ERPs in men and women at the analyzed channels are presented in Fig. 1. The P3b peak was measured by assessing its amplitude (i.e., size) and latency (i.e., timing). Amplitude (µV) was defined as the voltage difference between a pre-stimulus baseline and the largest positive-going peak of the ERP waveform within a P3b waveform latency window (250–500 ms). Latency (ms) was defined as the time from stimulus onset to the point of maximum positive amplitude within the P3b latency window. However, because there may be more than one positive peak in the P3b time window, manual inspection and correction of the P3b maximal amplitude value calculation process was applied as necessary to all ERP time courses. P3b waveform occurred as a broad positive peak in the latency range 300–600 ms, with its amplitude maximum up to 12 µV at around 350–400 ms (Fig. 1).
Gender-related differences in P3b distribution

Fig. 1. Grand averaged difference in ERPs elicited in the two-stimulus oddball experiment for men (black) and women (grey) at the analyzed 18 electrode locations.

Table I. Parameters of statistical analyses (parametric Student’s t-test and non-parametric Mann-Whitney U test) of P3b maximal amplitude and latency comparisons, for electrodes showing significant differences between genders ($p<0.05$).

<table>
<thead>
<tr>
<th>Channel</th>
<th>Student’s t-test results</th>
<th>Mann-Whitney U test results</th>
</tr>
</thead>
<tbody>
<tr>
<td>P7 – amplitude</td>
<td>$t_{18} = -3.09$, $p = 0.0063$</td>
<td>$Z_{corr} = -2.68$, $p = 0.0073$</td>
</tr>
<tr>
<td>F3 – latency</td>
<td>$t_{18} = 3.17$, $p = 0.0053$</td>
<td>$Z_{corr} = 2.43$, $p = 0.015$</td>
</tr>
<tr>
<td>FC1 – latency</td>
<td>$t_{18} = 3.42$, $p = 0.0031$</td>
<td>$Z_{corr} = 2.73$, $p = 0.015$</td>
</tr>
<tr>
<td>C3 – latency</td>
<td>$t_{18} = 3.23$, $p = 0.0047$</td>
<td>$Z_{corr} = 2.51$, $p = 0.012$</td>
</tr>
<tr>
<td>CP1 – latency</td>
<td>$t_{18} = 2.45$, $p = 0.025$</td>
<td>$Z_{corr} = 2.24$, $p = 0.025$</td>
</tr>
<tr>
<td>CP5 – latency</td>
<td>$t_{18} = 4.10$, $p = 0.00067$</td>
<td>$Z_{corr} = 2.86$, $p = 0.0043$</td>
</tr>
</tbody>
</table>
The potential was the lowest in the frontal region and increases through central and centro-parietal to parietal region, with its maximal values along the midline. N100, P200 and N200 components, which reflect sensory and early attention processes, were also visible. The averaged ERPs from men and women were similar in height and latency, however there were some differences, especially in frontal, central and centro-parietal regions. These gender differences within the right side of the P3b peak were notable and will be discussed in a subsequent section.

**Statistical analysis of amplitude and latency of P3b peak**

To determine the spatial distribution of the P3b waveform more accurately, statistical analyses of P3b amplitude and latency were performed. The P3b amplitudes and latencies from 18 channels (F3, Fz, F4, FC1, FC2, C3, Cz, C4, CP1, CP2, CP5, CP6, P3, Pz, P4, P7, P8 and POz) were analyzed. Six analyses each were run on amplitude and latency data, to obtain a full view on how the P3b parameters differ in men and women.

**Gender-related differences**

The first step was to compare P3b amplitudes and latencies between men and women, for each channel, using t-tests. Given that some of the data didn’t meet the assumption of normality of the data distribution (i.e. amplitude at CP6 [W₁₈=0.87, P=0.013] and P8 [W₁₈=0.9, P=0.04] across the entire sample; amplitude at FC1 [W₁₈=0.77, P=0.006] and Cz [W₁₈=0.83, P=0.034] and latency at P7 [W₁₈=0.84, P=0.041] and P8 [W₁₈=0.84, P=0.042] in men; latency at C3 [W₁₈=0.82, P=0.023], C4 [W₁₈=0.84, P=0.046] and CP6 [W₁₈=0.82, P=0.023] in women), parametric Student’s t-tests were followed by nonparametric Mann-Whitney U tests. Both tests yielded consistent results, showing significant differences between gender groups. In particular, amplitude was higher at the P7 site for women than men, and latency at F3, FC1, C3, CP1 and CP5 sites was shorter in women than men (see Table I).

**Hemispheric differences**

The second step of the analysis was to evaluate hemispheric differences in P3b amplitude and latency across the entire sample, and within men and women separately. The amplitudes and latencies from pairs of corresponding left-right sites (F3-F4, FC1-FC2, C3-C4, CP1-CP2, CP5-CP6, P3-P4 and P7-P8) were compared using paired sample t-tests. First, we evaluated the assumption of normal distribution of the differences. For data not meeting criteria for normality (i.e., latencies for F3-F4 [W₁₈=0.88, P=0.019], FC1-FC2 [W₁₈=0.67, P=0.00002], and CP1-CP2 [W₁₈=0.89, P=0.025] in the whole sample, and FC1-FC2 [W₁₈=0.78, P=0.0087] and CP1-CP2 [W₁₈=0.81, P=0.02] in men), nonparametric Wilcoxon tests were used. Significant differences in the whole experimental group were observed only in latencies for two channel pairs: FC1-FC2 and CP5-CP6. However, when the analysis was performed within the gender groups separately, significant differences in latency were noted for C3-C4 and in amplitude for the P7-P8 pair in women. Among men, there were significant differences in latency for F3-F4, FC1-FC2, CP1-CP2, and CP5-CP6 in men (see Table II).

Across the entire sample and in men, latency of the P3b component was shorter in the right hemisphere than the left. In women, however, latency was longer in the right hemisphere as compared to the left. In women, amplitude of the P3b component at the P8 electrode site (right hemisphere) was smaller than at P7 site (left hemisphere).

### Table II. Parameters of statistical analysis of P3b maximal amplitude and latency comparisons between corresponding electrodes in both hemispheres performed in the whole experimental group, as well as in men and women separately.

<table>
<thead>
<tr>
<th>Channel pairs</th>
<th>Whole experimental group</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>F3-F4</td>
<td>NS</td>
<td>L: (t_{0.022})</td>
<td>NS</td>
</tr>
<tr>
<td>FC1-FC2</td>
<td>L: (Z=2.42, P=0.016)</td>
<td>L: (Z=2.60, P=0.0093)</td>
<td>NS</td>
</tr>
<tr>
<td>C3-C4</td>
<td>NS</td>
<td>NS</td>
<td>L: (t_{0.046})</td>
</tr>
<tr>
<td>CP1-CP2</td>
<td>NS</td>
<td>L: (Z=2.07, P=0.038)</td>
<td>NS</td>
</tr>
<tr>
<td>CP5-CP6</td>
<td>L: (t_{0.0034})</td>
<td>L: (t_{0.0035})</td>
<td>NS</td>
</tr>
<tr>
<td>P3-P4</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
</tr>
<tr>
<td>P7-P8</td>
<td>NS</td>
<td>A: (t_{0.047})</td>
<td></td>
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</tbody>
</table>
Midline differences

Next, we tested whether observed differences in the P3b peak parameters were due to their location along the midline. To address this, we used repeated-measures ANOVA to test for differences in amplitudes and latencies among Fz, Cz, Pz and POz. Across the entire sample, the data met the normality assumption, but the sphericity assumption was not fulfilled. Therefore, the ANOVA analysis utilized three different corrections for violation of sphericity: G-G, H-F and lower-bound. In addition, to ensure that this violation did not influence the interpretation of results, multivariate tests for repeated-measures ANOVA were also conducted. All tests resulted in significant differences in amplitude (F3=6.85, P_G-G=0.0085, P_H-F=0.0074, P_lower-bound=0.017; multivariate: F3=8.38, P=0.0012), but not in latency (F3=0.02, P_G-G=0.97, P_H-F=0.98, P_lower-bound=0.88; multivariate: F3=0.043, P=0.99) between midline channels across the whole experimental group. Mean P3b amplitudes and latencies at Fz, Cz, Pz and POz electrodes in men and women are presented in Fig. 2. Differences between electrode sites are marked with an asterisk. Post-hoc test with Bonferroni correction resulted in significantly lower amplitude at Fz than at other electrode locations (P=0.017 compared to the Cz electrode, P=0.0004 compared to Pz, and P=0.02 compared to POz). Further, repeated-measures ANOVA performed in the two gender groups separately revealed significant amplitude differences in men (\text{Chi}^2\text{Friedman ANOVA}_{N=10,df=3}=21.6, P=0.00008), but no differences in women (\text{Chi}^2\text{Friedman ANOVA}_{N=10,df=3}=3.0, P=0.39). In men, latency data met assumptions for normality and also sphericity, so parametric repeated-measures ANOVA was used and yielded non-significant results (F3=1.71, P=0.19). In women, corrected ANOVA resulted in non-significant differences (F3=2.73, P_G-G=0.1, P_H-F=0.09, P_lower-bound=0.13), and this was confirmed by multivariate tests (F3=1.02, P=0.44). Although latency differences along the midline were not significant in either gender groups, the observed differences from frontal to parieto-occipital brain regions were notable. In particular, latency increased from POz to Fz among men, whereas in women latency increased from Fz to POz.

Channel differences

Next, we used repeated-measures ANOVA to compare P3b amplitudes and latencies at 18 channel locations, with channel as the within-subject factor (F3-POz) and gender as the inter-subject factor (men, women). Given that the assumption of variation in homogeneity was not met, we performed a non-parametric \text{Chi}^2\text{Friedman ANOVA}. The results were significant for amplitude and latency across the whole experimental group, and in men and women separately (Fig. 3). The same analysis was then performed for electrode clusters contain-
ing averaged signals over neighboring electrodes (i.e., F3-FC1, F4-FC2, C3-CP1, C4-CP2, CP5-P3-P7, CP6-P4-P8, Pz-POz). Results showed significant amplitude differences across the experimental group and in men, but not in women. Latency differences were significant in all groups (i.e., whole group, men, women; see Table III).

**Correlations**

Correlation analyses were then performed between P3b amplitude and latency, as well as between RT and these two electrophysiological parameters. There was a significant but weak correlation between parameters of the P3b peak across the whole experimental group (N=340, Spearman’s R =-0.17, P=0.0016), as well as in women (N=170, Spearman’s R =-0.21, P=0.005). This correlation was not significant among men. After including electrode sites, a significant strong negative correlation was observed between amplitude and latency only in women at two electrode sites: C4 (N=10, Pearson’s R =-0.81, P=0.0045) and P8 (N=10, Spearman’s R =-0.73, P=0.018).

A moderate positive correlation was observed between RT and amplitude across the whole experimental group at electrode site Cz (N=20, Pearson’s R =0.56, P=0.01). This correlation was not significant when testing men and women separately. A negative correlation between RT and latency was observed at the P4 location across the whole experimental group (medium, N=20, Pearson’s R =-0.51, P=0.02) as well as in women (medium-strong, N=10, Pearson’s R =-0.69, P=0.029). There were no other significant correlations between RT and electrophysiological parameters.

**Spatio-temporal changes of ERP**

Spatio-temporal changes in the P3b potential (i.e., peaking and subsiding during experimental task) are presented as voltage maps in Figs 4 and 5. These maps show the distribution of voltage changes on the scalp surface in different time points, measured from the stimulus onset until the suppression of the ERPs.
Evaluation of the maps showed that the P200 peak increased earlier (130 ms and 150 ms) and lasted longer (up to 200 ms and 160 ms) in women than in men, respectively. The spatial distribution of this potential was also different between genders. In women, the voltage started at Fz, spread through FC1, FC2, Cz, CP1 and CP2 at 180 ms time point, and ended at Cz, CP1, CP2 and Pz at 200 ms. In women, the highest amplitude was reached at 180 ms at Cz (2.79 µV). In men, in contrast, the potential started at Fz and FC1, and ended at Fz, FC1, and FC2 with maximal amplitude at 160 ms at the Fz channel (1.8 µV) (Fig. 4).

Although the P3b waveform started at the same time (260 ms) in women and men, and had a maximum at Pz at similar time point (390 in women and 370 in men), the time course differed in men vs. women. In women, the P3b waveform started at (1) Pz and then progressed through (2) POz, CP1, and CP2; (3) Cz, P3, and P4; (4) C3 and C4; (5) FC1 and FC2; (6) Cz, C3, C4, CP1, and CP2, and (7) ended at CP1. In men, the P3b waveform started at (1) Pz, P4, and POz; then (2) CP1, CP2 and P3; (3) FC2 and C4; (4) C3; (5) FC1 and F4; and (6) finished at centro-parietal electrodes, including CP1, CP2, Pz, and C4 (Fig. 5). Of note, there was a second potential peak, evident particularly in women around 500 ms, with a maximum at CP1 (4.88 µV).

When comparing the ERPs between men and women, there are notable differences in the later time range related to P3b waveform decrease. Among men, a second positive peak was observed in the frontal and fronto-central areas around 550–700 ms, but this peak was only evident on the right side. In central regions, the slope of decreasing P3b peak was faster at C3 than at the C4 site. At 600 ms, the potential amplitude at C3 was zero, while at C4 it was still around 1 µV. In centro-parietal regions, the potential decreased in the similar fashion for both sides at CP1-CP2, but at CP5-CP6, potential was lower than zero on the left side. Similar to C3-C4, the P3b waveform was higher on the right side compared to the left for the P3-P4 electrode pair. At P7 and P8, there was a negative peak noticed just after 300 ms, which started arising after 400 ms on both sides, with higher amplitude at P8 than at P7 around 650–680 ms. In women, the hemispheric differences were less pronounced. In particular, there was a negative peak in frontal regions, but a second peak was observed around 450 ms on both sides. In fronto-central areas, the P3b potential decrease had similar characteristics on both sides; however, the potential remained higher on the right side. For the P3-P4 electrode pair, the P3b waveform decreased more rapidly on the right side, with a clearly observed second maximum around 500 ms. Potential was still higher at P3 than at P4. Similar to what was observed in men, the ERPs had a negative course for the P7-P8 electrode pair on both sides, but potential peaked towards positive values around 400 ms and was subsequently more positive on the left side.

The observed differences in time-related changes of the ERP distribution between men and women led us to

![Fig. 5. Voltage maps on the scalp surface in subsequent points (260 ms, 400 ms, 460 ms, 490 ms) within the P3b time range, in men (left column) and women (right column). More lateralized P3b distribution was observed in men at 260-460 ms, and higher amplitude values were observed in women at 490 ms.](image-url)
apply a different statistical method than the aforementioned conventional comparison of maximal P3b amplitude and latency values. Due to the MCP, which arises from the fact that the effect of interest (i.e., a difference between experimental conditions) is evaluated for a large number of channel-time pairs, a nonparametric permutation cluster test was used. With a test for between-subjects EEG study, a null hypothesis about the probability distributions of the subject-specific averages is tested. This test involves all subject-specific averages drawn from the same probability distribution, regardless of the experimental condition, and combines neighboring values that are likely to be correlated (e.g., neighboring time points and/or spatial locations) to reduce the MCP. In the first step, a permutation cluster test was run on single sensor, which allowed us to

Fig. 6. A single sensor analysis results with temporal clustering statistics: grand averaged ERPs from men and women (with difference waveforms) and t-statistic graphs for the following channels: C3, CP5, CP1, CP2, P3 and P7. Black lines indicate a time range wherein a cluster was found. Bold black lines indicate a time range wherein the differences in the cluster were significant (P<0.05).
reject the null hypothesis ($P<0.05$), using a two-sided paired $t$-test. Fig. 6 presents grand averaged ERPs from men and women (showing differences waveforms) and $t$-statistic graphs for channels, which revealed significant results. After selecting a single sensor, the cluster-based permutation tests revealed a difference between men and women in the following channels: C3 (one cluster), CP5 (two clusters), CP1 (one cluster), CP2 (one cluster), P3 (one cluster; starting around 600 ms up to around 700 ms), and in channel P7 (one cluster; between 400 and 450 ms; bold lines). Results of the test are shown in Fig. 6. The test was run using a high threshold (6.0) to find strong, localized effects. After lowering the threshold (0.05) to evaluate weaker and more diffuse effects, significant clusters were found at CP5, CP1, CP2 and P3 electrode sites. In particular, significant effects began at 300 ms at CP5, around 400 ms at other locations, and up to around 800 ms (data not shown). In the second step, we performed a spatio-temporal cluster test with threshold=6.0, to take into account the spatial distribution of the sensor into the clustering procedure. This analysis yielded one spatio-temporal cluster ($P<0.05$) that contained C3, CP1, CP2, Cz, CP5, and P3 sensors between 543 and 714 ms (Fig. 7).

**Limitations**

Given that several components exist in ERP courses and these components often overlap, it is sometimes difficult to distinguish which peak maximum is generated by the P3b waveform. This is particularly difficult when negative components are present, and is noticeable at more anterior electrodes where the positive P3b peak may have negative maximal amplitude. To overcome this problem, we calculated difference waveforms (i.e., target-standard). Calculating the difference removed the influence of all other components that are not related to attention processes. Amplitude was defined as the voltage difference between a pre-stimulus baseline and the largest positive-going peak (i.e., positive or less negative – when the ERP was below the baseline) of the ERP waveform within a P3b waveform latency window (250 - 500 ms). However, there was often more than one positive peak in the P3b time window, so manual inspection and, if necessary, correction of the P3b maximal amplitude value automatic calculation process was applied to all ERP time courses. Therefore, after automatic calculation of the highest amplitude in the specified latency window, each ERP was manually inspected and, when the highest value appeared earlier than 300 ms, the value of P3b peak was manually inserted. To further check for fidelity of the correction, statistical analyses were repeated for the full dataset that included values that were uncertain (i.e., those which appeared when the positive peak was observed just after 300 ms and there was a chance that it was not a P3b waveform). Separate analyses were also carried out uncorrected data. Both sets of statistical analyses (i.e., uncorrected and with removed uncertain values) yielded the same results as the corrected analyses that are reported in this manuscript.

**DISCUSSION**

Gender-related differences in parameters of P3b waveform were observed only at electrode sites in the left hemisphere. In particular, we observed higher amplitude in women than men at electrode P7, and P3b latency was shorter in women than in men at electrode sites F3, FC1, C3, CP5, and CP1. These findings shed some light on discrepancies in previous studies of gender-related differences in the P3b potential. These data suggest that differences in the P3b waveform between men and women should be analyzed using a broader perspective than comparing amplitude and latency between gender groups. It also highlights how important the area size of EEG measurements is. For example, gender differences may be missed if recordings are only collected in midline or parietal electrodes.

Moreover, we found that the P3b latency across the whole experimental group differed between corresponding locations on the left and right side of the scalp in fronto-central (FC1-FC2) and centro-parietal
(CP5-CP6) regions, with the P3b potential maximum being faster in the right hemisphere. Interestingly, these hemispheric differences were not the same in men and women. In women, the only differences that were significant were a shorter latency at C3 than at C4 site, and a higher amplitude at P7 than P8. More hemispheric differences were noticed in men than in women. In particular, in frontal (F3-F4), fronto-central (FC1-FC2) and centro-parietal (CP1-CP2 and CP5-CP6) regions, P3b peaked faster on the right side. Given that the generation and transmission of the neural activations which induce the scalp P3b potential (i.e., attention processes in frontal and temporal/parietal brain regions), we obtained differences in its parameters along midline electrodes. These differences, however, were limited only to amplitude. Interestingly, latency did not significantly differ between Fz, Cz, Pz, and POz in any of the analyzed groups (Figs 2 and 3). By contrast, amplitude at Fz was lower than at all other electrode locations, in the entire group as well as in men. It is also notable that the latency increased on the midline differently in each group, although these effects did not reach significance. In men, latency increased from parieto-occipital to frontal, while in women: from frontal to parieto-occipital brain area. Consistent with the results of Conroy and Polich (2007), we observed an increase of P3b latency from frontal to parietal regions in women.

Spatial differences in P3b parameters were investigated further by analyzing temporal changes in potential distribution on the scalp in men and women. Differences were observed in the P200 potential, which started earlier and lasted longer in women than in men. Moreover, the P200 appeared more centrally in women, while in men it was distributed across frontal and fronto-central areas (Fig. 4). The P3b potential was also distributed differently in women than in men (Fig. 5). In women, the P3b was localized in general across central, centro-parietal, parietal, and parieto-occipital scalp regions. In men, in contrast, the P3b was more pronounced in the right hemisphere. These time-related changes of P3b waveform confirmed higher maximal P3b amplitudes on the right side in men throughout the whole scalp area, with no hemispheric differences between frontal to parietal regions in women (with the exception of the P7-P8 electrode, which was higher on the left side). Additionally, analysis of temporal changes in the ERPs showed that the P3b potential lasted longer in women, with a more distinct second maximum around 500 ms. The second peak may be due to an additional component. Interestingly, in the time range after P3b maximum, amplitude was higher on the right compared to the left side for women in fronto-central regions, and higher on the left compared to the right side in parietal areas. In men, in contrast, amplitude was always higher on the right side. Statistical spatio-temporal analysis of the ERP waveforms using nonparametric permutation cluster tests confirmed this lateralized character of a suppressing P3b waveform. These analyses yielded significant differences in ERP amplitude between men and women in the 543–714 ms time range in the centro-parietal and parietal scalp areas in the left hemisphere (Figs 6 and 7). These results suggest that surface P3b potential distributes differently in the time points following target stimulus onset in men versus women, with more pronounced lateralization towards the right side in men, and different behavior of these changes in women. Learmonth et al. (2017) observed right lateralization in response to long lines during a spatial attention ERP task in young people. The authors interpreted this result as arising from a right posterior-parietal dominance for visuospatial processing in young adults, resulting in a net asymmetry of activity between the right and left parietal cortices when performing spatial judgements (Learmonth et al., 2017). According to Roalf et al. (2006), the brains of men are typically more lateralized than those of women. While solving visual tasks, men showed a decrease in left hemispheric oxygenation and an increase in the right hemisphere (Roalf et al., 2006). Previous studies demonstrate that men process information more asymmetrically, whereas women rely on both hemispheres when processing verbal and spatial information (Kolb and Wilshaw, 1996; Kramer et al., 1996; Jaušovec and Jaušovec, 2009a). Similar asymmetries were observed in imaging studies, for example e.g., men showed significantly stronger parietal activation, while women showed significantly greater right frontal activation in a functional magnetic resonance imaging mental rotation task (Weiss et al., 2003). The observed gender differences may be attributed to morphological differences in brain structure and organization (e.g., corpus callosal neuroanatomical integrity and size, temporal-parietal junction integrity, or gray matter volumes), differences in allocation of attention, or the matching process between the presented stimulus and the internal representation of the stimulus relevant for the task (Hoffman and Polich, 1999; Kok, 2001; Merritt et al., 2007). Male brains were found to be more asymmetric than female in all brain areas, but especially in temporal areas, the thalamus, and the posterior cingulate cortex (Kovalev et al., 2003). Ingalhalikar et al. (2014) studied gender-related differences in the structural connectome of the human brain using diffusion tensor imaging. In all supratentorial regions, males had greater within-hemispheric connectivity, as well as enhanced modularity and transitivity. In females, however, between-hemispheric connectivity and cross-mod-
ule participation predominated. These observations were regarded by the authors as fundamental sex differences in the structural architecture of the human brain (Ingalhalikar et al., 2014). Our study documented a weak correlation between Pb3 maximal amplitude and latency in women and no correlation in men, when all electrodes were averaged. After taking electrode site into account, we found a strong negative correlation between Pb3 amplitude and latency only at P8 and C4 in women, and no significant correlations in men. Again, we can see the influence of lateral differences, as both electrodes are in the right central and parietal regions. Similarly, a relationship between these electrophysiological parameters and RTs were observed only in women at two electrode sites. In particular, we observed a medium correlation between Pb3 amplitude and RT at Cz, and a medium/strong negative correlation between RT and Pb3 latency at P4. Pb3 latency was assumed to be a measure of classification speed proportional to the time required to detect and evaluate a target stimulus, and is independent of behavioral response time (Polich and Herbst, 2000). As Halgren et al. (1995) pointed out, the Pb3 peak occurs at about the same latency as the subject’s response, indicating that the stimulus has been accurately classified (Halgren et al., 1995). Since the time from Pb3 onset to Pb3 peak is about equal to the time from motor command to behavioral response, the Pb3 may begin when the stimulus has been sufficiently processed to be accurately perceived. In a study by Volpe et al. (2007), there was no correlation between RT and current source density values observed in the regions activated for the Pb3, arguing against involvement of these regions in response selection processes. As the Pb3 component is largely independent from response selection and may primarily reflect stimulus categorization activity, some data indicate that Pb3 reflects the process of effortful attentional allocation and stimulus evaluation for task relevance (Volpe et al., 2007). Recently, two views on role of Pb3 latency in response evaluation have been introduced: stimulus-related and response-related (Walsh et al., 2017). The potential role of the Pb3 component in strategic processing is supported by the fact that Pb3 sometimes follows the response. In addition, there are often weak or absent correlations between Pb3 latencies and RTs, suggesting that the Pb3 does not directly relate to responses. However, other evidence indicates that the Pb3 plays a role in tactical processing. Taken together, the relationship between the Pb3 and responding remains controversial (Walsh et al., 2017). The tactical and strategic views both assume a relationship between stimulus categorization and the Pb3, but these views differ in whether they ascribe the Pb3 a role in immediate responses or future behavior. Our study is concordant with the strategic view; however, strong correlations in the right hemisphere observed in women may indicate a different character of response evaluation in males versus females.

CONCLUSIONS

In sum, we observed a non-equal spatial distribution of visual ERP waveforms on the scalp surface in a standard two-stimuli oddball paradigm. The highest Pb3 waveform was observed at midline parietal regions, and lowest in frontal regions, which is in the accordance with the known generators of Pb3 potential. Moreover, the spatial distribution of ERP signal on the scalp surface was more lateralized towards the right side in men, and more central in women. The Pb3 waveform in men peaked earlier in the right frontal-central and centro-parietal brain regions than their left counterparts. In contrast, the Pb3 waveform in women was earlier and higher at left central and parietal locations, compared to the right side. Gender-related differences in Pb3 amplitude and latency were observed only in left hemisphere. Of note, the differences observed in our study originated not only from differences in the largest Pb3 amplitude and latency, but also from the speed and character of the Pb3 fall, resulting in spatio-temporal amplitude changes. Moreover, hemispheric and temporal differences between men and women were observed in the spatial distribution of the P200 potential. These results suggest that gender-related differences evoked in visual two-stimulus oddball paradigm are complex, and include spatio-temporal changes in ERP waveforms generation, and distribution and suppression across the scalp, which may be related to early and late stages of attention processes.

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